

# PATENT

Docket No.: HMR2041 US NP1

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of  
**Kurt M. Kessler**

Examiner: Chang, C.

Art Unit: 1625

Serial No.: **09/760,590**

Filed: **January 16, 2001**

Title: Ethanol Solvate of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxy-8[4R-3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail in an envelope addressed to Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450, on

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### DECLARATION UNDER RULE 132

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, Gregory M. Shutske, declare that:

1. I received a B.S. in chemistry from Rose Polytechnic Institute, Terre Haute, Indiana, in 1971 and a Ph.D. in organic chemistry from the University of Indiana in 1975. I have been employed as a distinguished scientist at Aventis Pharmaceuticals Inc. and its predecessor companies, Hoechst Marion Roussel Inc. and Hoechst Roussel Pharmaceuticals Inc., since 1975. My research activities have been primarily in the field of organic chemistry and medicinal chemistry since about 1975. I am an author of about 55 peer-reviewed publications in the areas of organic chemistry and medicinal chemistry, and I am an inventor or co-inventor on about 65 U.S. patents.

2. I am an employee of Aventis Pharmaceuticals Inc. and I am not an inventor of the instant patent application. However, I have read the disclosures of the instant application and I am quite familiar with the disclosed and claimed subject matter therein.

3. I have also reviewed Kyoung Soon Kim U.S. patent 5,908,934 (Kim '934) and particularly column 9, Example 2-D, that describes the preparation of (3S-cis)-2-(2-chlorophenyl)-8-(3-hydroxy-1-methyl-4-piperidinyl)-5,7-dihydroxy-4H-1-benzopyran-4-one

that utilizes methodology and techniques well known to one of ordinary skill in the art of organic chemistry.

4. I have reviewed and understand the rejections of Claims 10-19 under 35 U.S.C. § 103(a) over Kim '934 in view of Cheronis and Evans, including the sentence of Example 2-D starting at column 9, line 53, of Kim '934 that reads "The precipitated solid was filtered, washed with ethyl ether three times and dried to afford a solid, 6.7 g which contained the title compound methanol." and is construed to be "consistent with the nomenclature of solvates/hydrates..." as is alleged by the examiner in the office action of November 6, 2002.

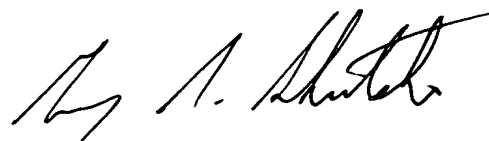
5. I believe certain portions of the Kim '934 Example 2-D to be ambiguous as written, most notably the phrase "title compound methanol" that appears in the sentence in column 9, starting at line 53, and reads "The precipitated solid was filtered, washed with ethyl ether three times and dried to afford a solid, 6.7 g which contained the title compound methanol." Although this affidavit is concerned with interpretation of the word "methanol" in the phrase "title compound methanol" of the quoted sentence, the phrase "title compound methanol" is the source of ambiguity for two reasons as will be discussed in paragraphs 6 and 7.

6. First, the quoted sentence discussed in paragraph 5 of this declaration implies that the "title compound" was obtained and the "title compound" of Example 2-D in Kim '934 is the name of the free base form of the compound. Careful reading of Example 2-D suggests that the "title compound hydrochloride" was obtained rather than the free base form of the compound. Supporting the fact that the "title compound hydrochloride" was obtained is an earlier description in Example 2-D of an acidification step with hydrochloric acid (Kim '934, column 9, lines 48-52). Further support that the "title compound hydrochloride" was obtained is provided by Kim '934's comparison of the melting point of the pale yellow solid obtained in column 9, line 58, to the literature reference 1 compound that is known to be the hydrochloride sesquihydrate form of the parent compound as is described in US 4,900,727 (reference 1). Thus the phrase "title compound" in the quoted sentence is ambiguous since it fails to properly describe the salt form of the compound that was obtained and this would suggest to one of ordinary skill in the art that an inadvertent omission of wording may have occurred within the phrase "title compound methanol".

7. The phrase "title compound methanol" discussed in paragraph 5 is also not written in explicit form that is consistent with art accepted or recognized language for the nomenclature of solvates or hydrates. Language to describe the solvate or hydrate form of a compound may be explicitly stated by several different art accepted or recognized phrases including "title compound methanolate", "title compound, methanol solvate", "title compound, compound with methanol", "title compound, compound with methanol (1:1)" [where the ratio of compound and solvent to each other is known and is illustrated by the designation (1:1)] and other such explicit phrases. Indeed the phrase "title compound methanol" may represent an incomplete description of the material obtained due to inadvertent omission of explicit wording not only with respect to the word "hydrochloride" as discussed in paragraph 6, but also with respect to art recognized description of a solvate as discussed in this paragraph. Thus, it is not possible for one skilled in the art to conclude with any certainty that a methanol solvate or clathrate was obtained from the phrase "title compound methanol" without additional supporting spectral data or physical evidence (e.g. elemental analysis), and Kim '934 does not provide such supporting data. Thus, one of ordinary skill in the art cannot confidently and unequivocally construe the sentence "The precipitated solid was filtered, washed with ethyl ether three times and dried to afford a solid, 6.7 g which contained the title compound methanol." to be "consistent with the nomenclature of solvates/hydrates." and the true form of the compound described as "title compound methanol" is not readily discernable from the description provided.

8. As a person signing below, I hereby declare that all statements made herein are of my own knowledge, are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signed this 19th day of March 2003.



Gregory M. Shutske